Central Pontine Myelinolysis and Ataxia: an Unusual Manifestation of Hypoglycaemia

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Hypoglycaemia is common in people with diabetes who aim to achieve good blood glucose control. Severe hypoglycaemia presents with evidence of neurological dysfunction, such as inability to concentrate, confusion, siezures, and coma. Such disturbances are reversible on correction of the hypoglycaemia. Infrequently there may be a focal neurological deficit and we report one such case presenting with cerebellar symptoms following an episode of severe hypoglycaemia. A magnetic resonance scan showed features consistent with the presence of central pontine myelinolysis. The symptoms resolved within a few months with only minimal residual neurological deficit. © **1998 John Wiley & Sons, Ltd.**

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Hypoglycaemia is common in patients with diabetes mellitus but rare in the non-diabetic population. This is because of diabetes-related impairment of counterregulatory mechanisms. Such impairment is associated with increased duration of diabetes but defective symptomatic and counterregulatory responses to hypoglycaemia can also be induced by antecedent hypoglycaemia. This is believed to be the mechanism for the increased risk of severe hypoglycaemia seen in intensively treated patients with Type 1 diabetes in the drive for normoglycaemia.[1]

A major danager of hypoglycaemia is loss of brain function. The brain is almost exclusively dependent on its supply of glucose from circulation as there are negligible intracerebral glucose stores.[1] Hypoglycaemia thus produces a variety of neurological symptoms. Seizure was originally described by Golden in 1937.[2] Focal neurological deficit such as hemiplegia has also been reported,[3] as well as movement disorders such as choreoathetosis[4] and paroxysmal dyskinesia.[5] Central pontine myelinolysis has been described in one patient undergoing haemodialysis who had frequent and rapid changes of plasma glucose.[6] We report a case of central pontine myelinolysis presenting with ataxia and dysarthria, which occurred after an episode of severe hypoglycaemia.

Case Report

LG, a 24-year-old shop assistant, complained of feeling unsteady on her feet during a routine diabetes clinic consultation. Type 1 diabetes mellitus had been diagnosed at the age of 4 and as a teenager, she found it very difficult to control. Metabolic control had been poor for many years, with glycated haemoglobins as high as 17 % (non-diabetic reference range 3.5–6.8 %). The patient developed several chronic complications of diabetes. Necrobiosis lipoidica appeared in her legs during her teen years. At the age of 19, she developed painful neuropathy. Diabetic retinopathy required treatment with photocoagulation and vitrectomy, and visual impairment prevented her from driving. She also had proteinuria, although her plasma creatinine and serum electrolyte concentrations remained within the normal range. Later her general condition improved. Her visual acuity improved sufficiently for her to be able to drive and she managed to get a job. She developed a stable relationship. She expressed her desire to become pregnant. Despite her improved condition, her diabetes control was still very poor (HbA_1 21.7 %) and she was advised to improve the control of her diabetes before conceiving.

Following this her home blood glucose measurements fluctuated widely. During December 1995 she had a few episodes of hypoglycaemia with home glucose recordings below 2 mmol. She lost awareness of hypoglycaemia. On Boxing Day, she woke up around 3 am feeling unwell. She could not measure her blood glucose as she had run our of test strips and she went back to bed where she was found unconscious by her mother later in the morning. An emergency doctor injected intramuscular glucagon, resulting in return of consciousness. Following this episode she became unsteady on

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her feet but did not seek medical help. When seen in the diabetes clinic, she had slurred speech and mild cerebellar ataxia of the limbs. Reflexes were sluggish and plantars were equivocal. Romberg's sign was negative. She did not have any focal weakness nor was there any evidence of peripheral neuropathy. Serum sodium was 139 (reference range 130–147 mmol l^{-1}).

In view of the onset of symptoms following severe hypoglycaemia, a clinical diagnosis of cerebellar insufficiency following hypoglycaemia was made. Detailed examination by a neurologist confirmed this finding. MRI scan of the brain showed high signal intensity in the centre of the pons with some extension into the midbrain and medulla, typical of the changes seen in central pontine myelinolysis (Figure 1(a) and (b)).

Her symptoms resolved gradually. By 6 months her speech was normal. There was still some impairment on heel/toe walking.

Discussion

Central pontine myelinolysis (CPM) was first described in 1959 in hyponatraemic patients with a history of alcohol abuse.[7] It has been classically defined as symmetrical and selective destruction of myelin sheaths in the central portion of the basis pontis, without evidence of an underlying vascular lesion or signs of inflammation. The abnormality is demonstrable on CT and MR imaging, but the latter is more sensitive.

In the clinical setting, CPM has been described mainly in association with rapid correction of hyponatraemia, being reported both with hyponatraemia and hypernatraemia, hypokalaemia, liver transplantation, renal transplantation, severe liver disease, chronic alcoholism, malnutrition, anorexia nervosa, and hyperemesis gravidarum. At autopsy, clinically asymptomatic CPM has frequently been observed.[8]

Patients suffering from severe burns are susceptible to CPM.[9] McKee *et al*. found CPM during autopsy of such patients more often compared with that found in the general population. This was associated with prolonged periods of extreme hyperosmolality (at least 360 mOsm kg^{-1}) for at least 3 days. It was not associated with hyponatremia or its correction.

Cerebellar ataxia has been reported in some cases of CPM[10] and is mainly axial. Some cases involved abnormal limb movement and dysarthria. It is suggested that cerebellar symptoms are due to a cerebellar peduncular

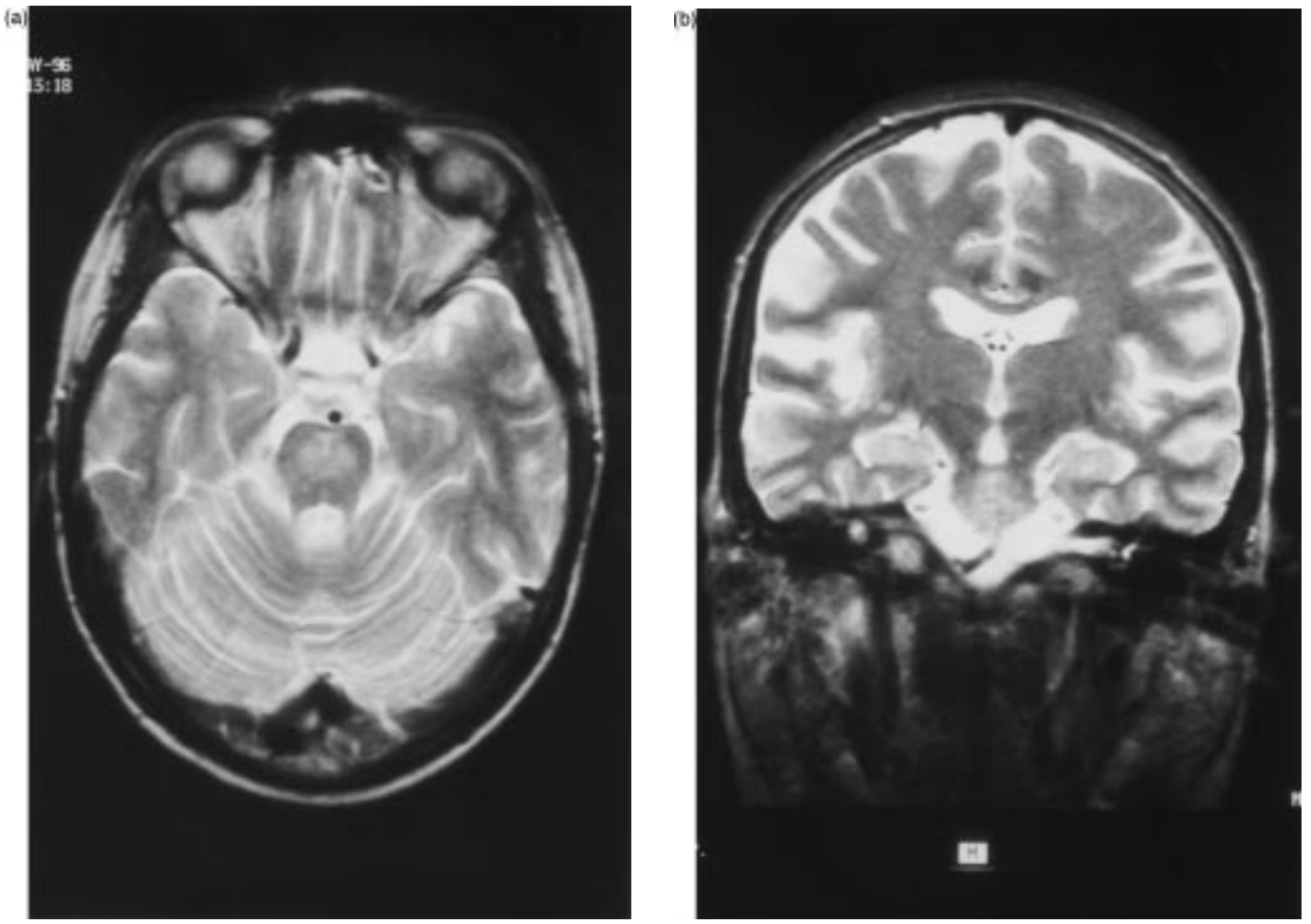

Figure 1. T2 weighted MRI image in (a) the axial and (b) coronal plane showing a large area of increased signal intensity in the centre of the pons

lesion or extrapontine cerebellar myelinolysis. In our case we could not demonstrate any cerebellar lesion apart from some atrophic changes disproportionate to her age.

It is not obvious why hypoglycaemia should produce focal neurological symptoms. In most cases of neruological disorder associated with severe hypoglycaemia, there is a non-focal presentation such as confusion, coma or seizures. Newman *et al*. described a case of choreoathetosis due to hypoglycaemia which recurred on subsequent episodes of hypoglycaemia. There was no structural lesion on CT scan.[4] On review of the literature, most patients with a focal neurological deficit have not shown any structural lesion on CT, although reversible CT abnormalities have been reported. In an animal study, Meyer and Portney demonstrated that hypoglycaemia produced localized reversible neurological deficits simulating stroke due to middle cerebral artery occlusion.[11] Shintani *et al*. demonstrated reversible hypoperfusion in the left hemisphere during a hypoglycaemic episode.[3] It is possible that the presence of a macrovascular or microvascular abnormality in a part of the central nervous system could be responsible for these reversible focal neurological deficits. On the other hand it is possible that the neuronal damage due to hypoglycaemia cannot be imaged by conventional imaging procedures.

In 1942, R.D. Lawrence described six fatal cases of hypoglycaemia where neuropathological examination showed degeneration and necrosis of nerve cells with glial proliferation involving different parts of the central nervous system.[12] Kalimo *et al*. also described necrotizing injury with gliosis after fatal hypoglycaemia, in various parts of the central nervous system.[13] Changes have been found in the cerebral cortex, basal ganglia, hippocampus and cerebellum. Necrotic foci measuring a few millimetres in diameter have been described in the pons.

This case demonstrates that, despite reassuring data from the DCCT,[14] hypoglycaemic brain injury is a serious potential complication of insulin therapy. It is possible that patients such as ours, with advanced microvascular complication may be at particular risk. Although generalized neurological symptoms are the usual manifestation of hypoglycaemia, physicians treating diabetes should be aware that unusual neurological syndromes may also occur.

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